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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/885,287	06/21/2001	Andreas Sewing	MERCK-2261	2670

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EXAMINER	
GOLLAMUDI, SHARMILA S	
ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 08/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/885,287	SEWING ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 21-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 21-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt of Request for Continued Examination and Amendments/Remarks received on June 5, 2004 is acknowledged. Claims **1-10 and 21-26** are pending in this application.

Specification

The objection to new matter in the specification is withdrawn upon further consideration and in view of applicant's remarks.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of claims 1-3 and 5-6 under 35 U.S.C. 102(b) as being anticipated by Sauk et al (4,780,450) is maintained.

Sauk et al disclose a composition containing particulate calcium phosphate (hydroxyapatite) and type I collagen (col. 4, lines 59-66). A mixture of type I and type III collagen is taught (example 1). Sauk et al disclose in column 2, line 60 to column 3, line 5, "the composition preferably comprise a mixture of phosphophoryn calcium, a matrix material (type I collagen), and calcium phosphate ceramic. These compositions are intended to facilitate matrix-mediated mineralization, whereby the collagen defines a structural matrix and the salt regulates and directs mineral deposition in terms of its location, crystallinity and association with the calcium phosphate ceramic particles.

Note that the recitation "coating for metallic implant materials" is intended use and is not given patentable weight. Further, the recitation "wherein the coating is obtained by precipitating phosphate from a solution in the presence of collagen" is a product-by-process limitation. According to the MPEP section 2113, "even though product by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production, if the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior art was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.Cir. 1985).

In regards to claim 3, collagen in combination with mineral components inherently tends to separate phases or layers. US Patent 5,543,441 column 3 lines, 66 to column 4, line 5 is cited as art of interest to support examiner's inherency argument.

Response to Arguments

Applicant argues that applicant's collagen matrix, which is mineralized with calcium phosphate by precipitating calcium phosphate from a solution in the presence of collagen and has definite physical properties, i.e. permeability.

Applicant's arguments have been fully considered but they are not persuasive. The examiner points out that the claims rejected are product claims; therefore the newly added product-by-process limitation does not hold patentable weight. As stated above, a product-by-process limitation is only given weight if it yields a different structure from the prior art. In instant case, it does not since both the prior art teach a composition containing the recited components a collagen matrix mineralized with calcium phosphate. Applicant has not provided

any evidence to prove a structural difference. Thus, there is no structurally distinguishing feature compared to the prior art and the rejection is maintained.

Rejection of claims 1-3 and 5-8 under 35 U.S.C. 102(b) as being anticipated by Geistlich et al (5,573,771) is maintained.

Geistlich et al disclose a bone mineral product containing bone, collagen, and gelatin (examples and claims 1 and 8). The macromolecular material used to provide the matrix is made of gelatin and Type I collagen or a mixture of type I-III. See column 2, lines 41-43. The reference discloses that the natural bone used contains calcium phosphate, brushite, whitlockite, and octa-calcium phosphate (col. 1, lines 30-31). A pharmaceutical agent is absorbed in to the bone mineral. See column 3, lines 20-60 and claim 3. Claim 5 discloses the pharmaceutical agent is a growth factor.

Note that the recitation "coating for metallic implant materials" is intended use and is not given patentable weight. Further, the recitation "wherein the coating is obtained by precipitating phosphate from a solution in the presence of collagen" is a product-by-process limitation. According to the MPEP section 2113, "even though product by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production, if the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior art was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.Cir. 1985).

In regards to claim 3, collagen in combination with mineral components inherently tends to separate phases or layers. US Patent 5,543,441 column 3 lines, 66 to column 4, line 5 is cited as art of interest to support examiner's inherency argument.

Response to Arguments

Applicant argues that applicant's collagen matrix, which is mineralized with calcium phosphate by precipitating calcium phosphate from a solution in the presence of collagen and has definite physical properties, i.e. permeability.

Applicant's arguments have been fully considered but they are not persuasive. The examiner points out that the claims rejected are product claims; therefore the newly added product-by-process limitation does not hold patentable weight. As stated above, a product-by-process limitation is only given weight if it yields a different structure from the prior art. In instant case, it does not since both the prior art teach a composition containing the recited components a collagen matrix mineralized with calcium phosphate. Applicant has not provided any evidence to prove a structural difference. Thus, there is no structurally distinguishing feature compared to the prior art and the rejection is maintained.

Rejection of claims 1-3, 5, 7-10, and 22-23 under 35 U.S.C. 102(b) as being anticipated by Rhee et al (5,543,441) is maintained.

Rhee et al teach implants coated with collagen-polymer conjugates. The composition contains collagen (Type I) and hydroxyapatite/tricalcium phosphate or gelatin beads (example 7). The dried collagen-PEG composition has sponge-like properties and when incorporated with growth factors, serve as an effective controlled-release device. See column 7, lines 1-6. Example 5 discloses coating a titanium implant with eh coating composition.

Note that the recitation "coating for metallic implant materials" is intended use and is not given patentable weight. Further, the recitation "wherein the coating is obtained by precipitating phosphate from a solution in the presence of collagen" is a product-by-process limitation. According to the MPEP section 2113, "even though product by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production, if the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior art was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.Cir. 1985).

In regards to claim 3, collagen in combination with mineral components inherently tends to separate phases or layers. US Patent 5,543,441 column 3 lines, 66 to column 4, line 5 is cited as art of interest to support examiner's inherency argument.

Response to Arguments

Applicant argues that applicant's collagen matrix, which is mineralized with calcium phosphate by precipitating calcium phosphate from a solution in the presence of collagen and has definite physical properties, i.e. permeability.

Applicant's arguments have been fully considered but they are not persuasive. The examiner points out that the claims rejected are product claims; therefore the newly added product-by-process limitation does not hold patentable weight. As stated above, a product-by-process limitation is only given weight if it yields a different structure from the prior art. In instant case, it does not since both the prior art teach a composition containing the recited components a collagen matrix mineralized with calcium phosphate. Applicant has not provided

any evidence to prove a structural difference. Thus, there is no structurally distinguishing feature compared to the prior art and the rejection is maintained.

Claims 1-3, 5, 9-10, 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Worch et al (6,524,718).

Worch et al disclose a metallic substrate (titanium) having a polyphase oxide coating. The polyphase coating has a metal oxide and at least one other organic or inorganic phase. See abstract. The process of coating the implant yields a two-layer oxide coating, where the outer layer is the inorganic and/or the organic phase. See column 2, lines 32-45. The inorganic component is calcium phosphate and the organic component is Type I collagen. See column 2, lines 46-60. Example 1 discloses a coating thickness of 250 nm (.250 micrometers).

Note that the recitation "coating for metallic implant materials" is intended use and is not given patentable weight. Further, the recitation "wherein the coating is obtained by precipitating phosphate from a solution in the presence of collagen" is a product-by-process limitation. According to the MPEP section 2113, "even though product by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production, if the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior art was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.Cir. 1985).

Claims 1-4, 9-10 and 21-23 are rejected under 35 U.S.C. 102(b) as being anticipated by Shirkanzadeh (5,205,921).

Shirkanzadeh discloses a method of depositing bioactive coatings on conductive substrates wherein a cathode and D.C. potential is applied to raise the interfacial pH at the cathode sufficiently enough to precipitate the desired oxide or phosphate thereon as a dense adherent film. See abstract. The substrate can be titanium alloy or steel and the coating is 50 microns thick for a uniform, continuous, and firmly bonded coating. See example 4. The coating composition includes calcium phosphate and non-toxic biological compounds, i.e. collagen. The inorganic compounds, i.e. calcium phosphate, may be co-precipitated with the organic compounds, i.e. collagen. This process allows the doping of specific ions in calcium phosphate crystals. See column 3, lines 5-20. Preferably crystalline calcium phosphate is utilized compared to amorphous calcium phosphate. The particle range of the calcium phosphate is 2-5 microns. See example 2. The micropores in the calcium phosphate compound coating also encourage better adhesion of collagen. The instant doping agents (carbonate and fluoride) are taught in the electrolyte solution.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.

2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 5, 7-8, and 24-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shirkanzadeh (5,205,921).

Shirkanzadeh discloses a method of depositing bioactive coatings on conductive substrates wherein a cathode and D.C. potential is applied to raise the interfacial pH at the cathode sufficiently enough to precipitate the desired oxide or phosphate thereon as a dense adherent film. See abstract. The substrate can be titanium alloy or steel and the coating is 50 microns thick for a uniform, continuous, and firmly bonded coating. See example 4. The coating composition includes calcium phosphate and non-toxic biological compounds, i.e. collagen. The inorganic compounds, i.e. calcium phosphate, may be co-precipitated with the organic compounds, i.e. collagen. This process allows the doping of specific ions in calcium phosphate crystals. See column 3, lines 5-20. Preferably crystalline calcium phosphate is utilized compared to amorphous calcium phosphate. The particle range of the calcium phosphate is 2-5 microns. See example 2. The instant doping agents (carbonate and fluoride) are taught in the electrolyte solution.

The reference does not specify the type of collagen utilized, the diameter of the calcium phosphate crystals, or drugs.

Kwan et al teach a mineralized Type I collagen matrix containing calcium phosphate for bone grafting. Kwan teaches the suitability of collagen or collagen derivatives for the matrix, with a preference for Type I. The matrix may contain other agents such as growth factors, calcitonin, and binders such as gelatin. See column 3, lines 56-65 and column 4, lines5-10. By

utilizing drugs such as growth factors in the matrix, the matrix may also provide a substrate to which the host's growth factors may bind and facilitate repair. See column 5, liens 46-60. Kwan teaches that the particles are of an average diameter of less than five microns since these particles are small enough to phagocytized to stimulated local reaction and further bone resorption. See column 5.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings Shirkanzadeh et al and Kwan et al since both teach collagen matrix containing calcium phosphate. One would be motivated to look to the guidance of Kwan et al and utilize instant collagen type since the instant collagen type is recognized as suitable material for implants.

Further, one would be motivated to utilize instant active agents such as growth factors to facilitate repair. Therefore, the selection of the pharmaceutical contained in the implant depends on the intended use of the implant and the treatment plan.

Lastly, it is deemed obvious to one of ordinary skill in the art at the time the invention was made to manipulate the parameters of particle size of the calcium phosphate thorough routine experimentation, absent evidence to the contrary. Additionally, one would be motivated to utilize the instant diameter range since Kwan teaches the utilization of particles with less than 5 microns to further bone resorption.

Conclusion

No claims are allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

SSG

MICHAEL G. HARTLEY
PRIMARY EXAMINER